

SN 09/331,376  
Amendment filed May 27, 2003  
Response to Office Action mailed Feb. 26, 2003

The following listing of claims replaces all prior versions and listings of claims in the application:

**Listing of Claims:**

1. (previously amended) Method to detect and phenotype target cells in cell suspensions by using particles coated with antibodies directed against antigenic determinants/receptors expressed on the target cells, wherein 2 to 6 antibodies, each conjugated to a particle, wherein the particle is a fluorescent or dyed particle, are incubated under gentle rotation for about 5 minutes to about 2 hours with cell suspensions containing the target cells at 0°C to 25°C, followed by an enrichment procedure, and evaluation of the target cell rosettes microscopically and/or by suitable visualizing or imaging devices, wherein the cells are evaluated while in suspension, and wherein one antibody is conjugated to one type of particle instrumentally or visually separable by fluorescence, color and size, with sizes of the particles ranging from 0.01µm to 6µm, each antibody of the 2 to 6 antibodies is conjugated to different particles, and the ratio between the number of particles and the number of cells ranges from 0.5 : 1 to 20 : 1 in the cell suspension.

2. (previously amended) Method according to claim 1, wherein the said size of the particles ranges from about 0.5µm to about 4.5µm, the said ratio is 5 : 1 (number of particles/number of cells), the said incubation time is 30 minutes and the said incubation temperature is 4 ° C.

3. (previously amended) Method according to claim 1, wherein the particles used in the method are separable by a combination of fluorescence and/or size or a combination of fluorescent emission spectra, different colors or different sizes.

4. (previously amended) Method according to claim 3, wherein the particles used are separable by a combination of fluorescent emission spectra and/or size.

5. (canceled)

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6. (previously amended) Method according to claim 7, wherein the particles used in the method are coated with antibodies directed against the receptors/antigens selected from the group consisting of integrins, ICAM-1 (CD54), VCAM-1, NCAM (CD56), HCAM, LCAM, CD44, CD44 variants, ELAM-1, E-selectin, P-selectin, LFA (CD58), MACAN-1, E-cadherin, P-cadherin, tenascin, thrombospondin receptor (CD36), VLA-2, T-antigen, Tn-antigen, sialyl Tn, galbl-4GlcNac (nL4, 6, 8), gastrointestinal cancer antigen, Le<sup>y</sup>, di-Le<sup>x</sup>, tri Le<sup>x</sup>, CA15-3 epitope, CEA, lacto-N-fucopentanose III (CD15), GD<sub>3</sub>, GD<sub>2</sub>, Gb<sub>3</sub>, GM<sub>3</sub>, GM<sub>2</sub>, FucGM<sub>1</sub>, EGF receptor, c-erbB-2 (HER2), PDGF $\alpha$  receptor, PDGF $\beta$  receptor, transferrin receptor, NGF receptor, IL-2 receptor (CD25), c-kit, TNF receptor, high molecular weight melanoma antigen (HMW 250,000), MW 105 melanoma glycoprotein, MW100 kDa antigen (melanoma/carcinoma), gp 113, p95-100, gp75/TRP-1, gp 100-107, MAA, MW125kD (gp125), MAGE 1, MAGE 2, MAGE 3, tyrosinase, TP-1 epitope, Tp-3 epitope, MW 200kD sarcoma antigen, MW160kD sarcoma antigen, EGP-2 (cluster 2 epithelial antigen), MUC-1 antigens, MUC-2, MUC-3, LUBCRU-G7 epitope (gp 230kD), prostate specific antigen, prostate cancer antigen, prostate high molecular antigen (MW>400kD), polymorphic epithelial mucins, prostate specific membrane antigen (Cyt-356), human milk fat globin, 42kD breast carcinoma epitope, MW > 10<sup>6</sup> mucin, ovarian carcinoma OC125 epitope (MW 750 kD), pancreatic HMW glycoprotein, colon antigen Co-17-1A (MW 37000), Ga 733.2, TAG 72, pancreatic cancer marker, pancarcinoma marker, prostate adenocarcinoma-antigen, MW 150-130kD adenocarcinoma marker, MW 92kD bladder carcinoma marker, MW 600kD bladder carcinoma marker, bladder carcinoma antigen, hepatocellular carcinoma antigen, MW 48kD colorectal carcinoma marker, colon specific antigen, lung carcinoma antigen MW 350-420kD, colon cancer marker, bladder carcinoma antigens, neuroblastoma epitope, Mel-14 epitope, HMW 250kD glioma antigen, MW 18-22kD head and neck cancer antigen, HLA Class 1 antigen, HLA-A, HLA-B, HLA-A2, HLA-ABC, HLA-DR, HLA-DQ, HLA-DP,  $\beta$ 2-microglobulin, Fas (CD95/APO-1), FAsL, P75, cathepsin D, neuroglandular antigen (CD63), pan-human cell antigen, motility related antigens, proliferation markers, differentiation markers, drug resistance-related markers,

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angiogenesis markers, chemokine receptor markers, invasion-related antigens, B-cell CD antigens, and T-cell CD antigens.

7. (previously amended) Method according to claim 1, wherein the antigenic determinants/receptors expressed on the target cells are tumor antigens.

8. (previously amended) Method according to claim 7, wherein the tumor antigens are MOC31 anti EGP2 (anti-epithelial cell marker) antibody, anti-breast mucin (MUC1) antibody (BM7), 595, anti-EGF receptor (425.3), anti-erbB2 and anti-HMW melanoma antigen (9.2.27).

9. (previously amended) Method according to claim 1, wherein phenotyping of the target cells is performed, the phenotyping comprising profiling the antigenic determinants or receptors expressed on the cell membrane of the target cells.

10. (previously amended) Method according to claim 9, wherein target cell characteristics of biologically informative markers of diagnostic, prognostic and therapeutic value are registered.

11. (previously amended) Method according to claim 10, wherein the target cells are malignant cells.

12. (canceled).

13. (currently amended) Method according to claim 10, wherein the biological markers are E-cadherin, EGFr, c-erbB2, IL-2 receptor, TNF receptor-, EGP2, MUC1, MUC2 & 3, PSA, PSM, GA733.2, TAG72, 15-3 epitope, ovarian carcinoma CA- 125 epitope, Le<sup>y</sup>, CEA, 15-3 epitope, HMW 250000 melanoma antigen, gp 75/TRP-1, p95, MAG 1, MAG 2, MAG 3, TP 1 and TP 3 epitopes, Mel-14 epitope, Fas, FasL, p75, KAT-1, AMF, gp120, MUC 18, TA99, MDR, MRP, VEGFr, bFGF, CCR, CXCR, uPAR, uPA, PAI-1, TIMP1 & 2, MMP9, stromelysins, and cathepsin D and pan-human epitope.

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Claim 14. (previously added) Kit to detect and phenotype target cells in cell suspensions by using particles coated with antibodies/ligands directed against antigenic determinants/receptors expressed on the target cells, wherein 2 to 6 antibodies or ligands each conjugated to a particle, wherein the particle is a fluorescent or dyed particle, are incubated under gentle rotation for 5-10 minutes to 2 hours with cell suspensions containing the target cells at 0°C to 25°C, followed by an enrichment procedure, and evaluation of the target cell rosettes microscopically and/or by suitable visualizing or imaging devices, wherein the kit comprises particles conjugated to antibodies/ligands, wherein one antibody is conjugated to one type of particle instrumentally or visually separable by fluorescence, color and size, with sizes of the particles ranging from 0.01µm to 6µm, each antibody of the 2 to 6 antibodies is conjugated to the same or different particles, and the ratio between the number of particles and the number of cells ranges from 0, 5 : 1 to 20 : 1 in the cell suspension.

15. (previously added) Method according to claim 1, wherein the target cells are animal cells or human cells.

16. (previously added) Kit according to claim 14, wherein the target cells are animal cells or human cells.

17. (previously added) Method to detect and phenotype intact target cells in cell suspensions by using particles coated with antibodies directed against membrane-associated antigenic determinants/receptors expressed on the intact target cells, wherein 2 to 6 antibodies, each conjugated to a particle, wherein the particle is a fluorescent or dyed particle, are incubated under gentle rotation for about 5 minutes to about 2 hours with cell suspensions containing the intact target cells at 0°C to 25°C, followed by an enrichment procedure, and evaluation of the intact target cell rosettes microscopically and/or by suitable visualizing or imaging devices, wherein the cells are evaluated while in suspension, and remain intact, and wherein one antibody is conjugated to one type of particle instrumentally or visually separable by fluorescence, color and size, with sizes of

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the particles ranging from  $0.01\mu\text{m}$  to  $6\mu\text{m}$ , each antibody of the 2 to 6 antibodies is conjugated to different particles, and the ratio between the number of particles and the number of cells ranges from 0.5 : 1 to 20 : 1 in the cell suspension.